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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,508	03/26/2004	Xing Cheng	26-003820US	8613

7590 12/05/2006

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,508	CHENG ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,10-12,14-16,19,20,35,39,46-48,53,60,66,67 and 70-73* is/are pending in the application.

4a) Of the above claim(s) *35,39,46-48,53,60 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,10-12,14-16,19,20,67 and 70-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 25, 2006 has been entered.

Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 35, 39, 46-48, 53, 60, 66, 67 and 71-73 are pending. Claims 35, 39, 46-48, 53, 60 and 66 are withdrawn from consideration being drawn to non-elected subject matter. Claims 1, 2, 4, 6, 10-12, 14-16, 19, 20, 67 and 71-73 are under examination with respect to SEQ ID NO: 1, 9 and 10, respectively.

Response to Amendment

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, is withdrawn in view of Applicant's amendment clarifying the amino acid substitutions.

The rejection of claims 67-71 under 35 U.S.C. 102(b) as being anticipated by Karron *et al.* (*PNAS USA*, 1997, 94:13961-13966, "Karron"), is moot in view of cancelled claims 68 and 69, and withdrawn with respect to claims 67, 70 and 71, in view of Applicant's amendment. The claims now require that the polynucleotide molecule have at least 500, or at least 1000 contiguous nucleotides of SEQ ID NO: 1. As evidenced by Applicant's Exhibit G, an alignment

of the polynucleotide taught by Karron and the instant SEQ ID NO: 1 reveals that there are no regions of at least 500 or at least 1000 contiguous nucleotides. Therefore, Karron fails to teach or fairly suggest the subject matter of claims 67, 70 and 71.

Claims Summary and Interpretation

The claims are drawn to an isolated or recombinant nucleic acid molecule (DNA, cDNA, RNA or an artificial nucleic acid) comprising a polynucleotide sequence selected from the group consisting of:

(a) the full length SEQ ID NO: 1 or a complement thereof,

(b) a polynucleotide sequence greater than 97.8% identical to SEQ ID NO: 1 or a complementary sequence thereof, wherein the polynucleotide sequence encodes an infectious, replicating respiratory syncytial virus, and,

(c) a polynucleotide sequence encoding an amino acid sequence or unique subsequence selected from the group consisting of an amino acid sequence greater than 99.5% identical to SEQ ID NO: 9, and an amino acid sequence greater than 96.4% identical to SEQ ID NO: 10, wherein an RSV that comprises the amino acid sequence is infectious and replicating.

Specifically, the nucleic acid molecule of (b) is at least 98.5% identical to SEQ ID NO: 1, or a complementary sequence thereof. In another embodiment, the nucleic acid molecule has at least one artificially mutated nucleotide, such as a deleted, inserted or substituted nucleotide. The mutation is located in the open reading frame encoding the polypeptide of SEQ ID NO: 10. Specifically the deletion in SEQ ID NO: 10 is a mutation of amino acid residue 1, 4, 10 or a

combination thereof. In another embodiment, the open reading frame of SEQ ID NO: 10 is deleted.

Similarly, the polypeptide encoded by the polynucleotide of (c) comprises at least one deleted, inserted or substituted amino acid residue. The substitutions are listed in newly amended claim 11.

The unique polynucleotide subsequence of the polynucleotide of (c) comprises at least one complete ORF, such as SEQ ID NO: 9 and 10, or a plurality of complete ORFs.

Newly amended claim 67 is drawn to an isolated or recombinant nucleic acid comprising at least one unique polynucleotide subsequence comprising at least 500 contiguous nucleotides of SEQ ID NO: 1 or a complementary sequence thereof, with the proviso that the unique sequence includes at least one subsequence not included in SEQ ID NO: 14-19 or a complementary sequence thereof. More specifically, the subsequence comprises at least 1000 contiguous nucleotides of SEQ ID NO: 1. Also embodied is a subsequence that encodes at least 20, at least 50, at least 100, or at least 200 contiguous amino acid residues of SEQ ID NO: 9 or 10. Further, the subsequence encodes at least 50 contiguous amino acid residues of SEQ ID NO: 10. In another embodiment, the subsequence comprises at least one polynucleotide subsequence from a different strain of virus, or at least one polynucleotide subsequence from a different strain of human RSV, or at least one subsequence from a different species of virus.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 6, 10, 11, 12, 14, 15, 16, 19, 20, 67 and 70-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1(a) recites, "SEQ ID NO: 1 or a complementary polynucleotide sequence thereof". It is unclear whether Applicant intends to claim a fragment of the complementary sequence or the full complement. If the full complement is intended, suggested language is, "SEQ ID NO: 1 or the complementary polynucleotide sequence thereof" [emphasis added].

Similarly, claim 1(b) recites, "a polynucleotide sequence that is greater than 97.8% identical to SEQ ID NO: 1 or a complementary polynucleotide sequence thereof". If the full complement is intended, suggested language is, "a polynucleotide sequence that is greater than 97.8% identical to SEQ ID NO: 1 or the complementary polynucleotide sequence thereof" [emphasis added]. If the claim is amended as suggested, part (b) of claim 1 will be understood to encompass a polynucleotide sequence that is greater than 97.8% identical to the full-length SEQ ID NO: 1, or the full-length complement thereof.

Throughout the claims that are included in this rejection, the same question of whether Applicant intends to claim a fragment of the full-length complementary sequence or the full complement is raised. Clarification/correction is required to overcome this rejection.

The rejection of claims 1, 2, 4, 6, 10, 11, 12, 14, 15, 16, 19 and 20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The claims are summarized above. The claims encompass a large genus of polynucleotide sequences that have not been adequately described such that one of skill in the art would be in possession of the full scope of the invention as claimed.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant points to *Invitrogen v. Clontech*, 429 F.3d 1052 (Fed. Cir. 2005) as applicable to the present situation. Applicant argues that the genomic viral sequence and several viral protein sequences for RSV B 9320 are disclosed in the application. In *Invitrogen*, the issue revolved around a mutant reverse transcriptase with DNA polymerase activity but without RNase H activity derived from a variety sources. The disclosure of the representative species was limited to several deletion mutants of MMLV reverse transcriptase. Applicant notes that the Federal Circuit determined that the written description for the claimed polypeptides had been met because the sequences of reverse transcriptase genes were known, the genes of different species share significant homologies, and there was a known correlation between RNase H activity of reverse transcriptase and the structure of the gene encoding the reverse transcriptase. Applicant notes that homologous sequences in other strains of RSV were known in the art, and that sequence alignments between homologous sequences reveal conserved region that are more likely to be essential to the function of the protein than other regions of the protein.
    - In response to Applicant's arguments, there is a significant difference between the scenario of *Invitrogen* and the instant invention. In *Invitrogen*, adequate written

description was found for a polypeptide encoding a single protein: a reverse transcriptase. In contrast, the instant claims are directed to a polynucleotide molecule variant of SEQ ID NO: 1 that is able to encode an infectious, replicating RSV. While it is true that portions of various RSV strains share homology and share general structure similarities, the diversity between the numerous individual proteins within the virus must be taken into account. This is different than accounting for the differences in a single protein, such as reverse transcriptase. Thus to compare *Invitrogen* with the instant claims is to compare a single gene (RT) and a genome comprised of multiple genes encoding a complex structure (virion).

- The Office acknowledges that sequences of RSV are known and that there are sequence homologies between RSV strains. However, there is no known correlation between variants of SEQ ID NO: 1 and the function of encoding an infectious, replicating respiratory syncytial virus. Without guidance from Applicant, one would not know where to mutant within the 15,000 nt base sequence of SEQ ID NO: 1 such that the claimed function is retained. While regions can be identified that will encode various proteins, Applicant's claims encompass modifications of any kind anywhere along SEQ ID NO: 1.

- Applicant points to Smith *et al.* (*Protein Engineering*, 2002, "Smith") as an example of how sequence alignments of the F protein can be used to determine 3-D structures and thereby derive locations of certain functional components in a protein. Applicant also points to Garcia *et al.* (*J. Virology*, 1994, "Garcia") which shows an alignment of the G

proteins of many different RSV isolates. Applicant argues that the skilled artisan would readily deduce that locations having amino acid variability may be modified without losing the viability of the resulting virus. Applicant points to Fearns *et al.* (*J. Virology*, 2000, "Fearns"), showing a functional analysis of the promoters of human RSV by determining the effects of increasingly large deletion in the viral genome. Zimmer *et al.* (*J. Virology*, 2002, "Zimmer") disclose a structure function analysis relating to proteolytic processing of the F protein. Zimmer shows that mutations in one of the cleavage sties of the F protein abolished proteolytic processing at that site and the resulting virus, though viable, showed reduced cytopathic effect.

- In response to Applicant's arguments, the Office has considered the information provided in the references cited. The Office acknowledges that there are sequence similarities and regions that may be identified between RSV strains, thus their classification as RSV strains. However, Applicant's claims encompass modifications of any kind anywhere along SEQ ID NO: 1, as opposed to specific regions that are available for modification. The references that Applicant cited are evidence that certain proteins, such as the F and G protein can be modified to achieve certain specific functions. However, modifications along the entire SEQ ID NO: 1 that result in an infectious and replicating RSV have not been described. The fact that other RSV strains have sequence homology to SEQ ID NO: 1 does not identify which regions are available for modification other than those that are already identified in the existing strains. Furthermore, the claimed variants encompass modifications across the entire sequence, as opposed to the

modifications disclosed in the cited references that focus on particular regions for mutagenesis. Therefore, the rejection is maintained for reasons of record.

Conclusion

SEQ ID NO: 1 is free of the prior art of record.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 11/30/06

STACY B. CHEN
PRIMARY EXAMINER